Docket No.: ISIS-4789 Appln. No: Not yet assignate: Oligonucleotides Having A-DNA Form a DNA Form onformational Geometry
Inventor(s): Manoharan, et al
Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 1 of 9

Figure 1

Docket No.: ISIS-4789 Appln. No: Not yet ass

Title: Oligonucleotides Having A-DNA Form and B-DNA Form

Inventor(s): Manoharan, et al

Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 2 of 9

Figure 2

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e: Oligonucleotides Having A-DNA Form and -DNA Form

Conformational Geometry

Inventor(s): Manoharan, et al Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 3 of 9

Figure 3

Docket No.: ISIS-4789 Appln. No: Not yet assigned ligonucleotides Having A-DNA Form and Constraint Geometry

Inventor(s): Manoharan, et al

Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 4 of 9

FFECT OF CHEMICAL MODIFICATION ON THE STABILITY OF ISIS 11061 ONGENORS IN MOUSE PLASMA 1 HR AFTER IV BOLUS (5 mg/kg)

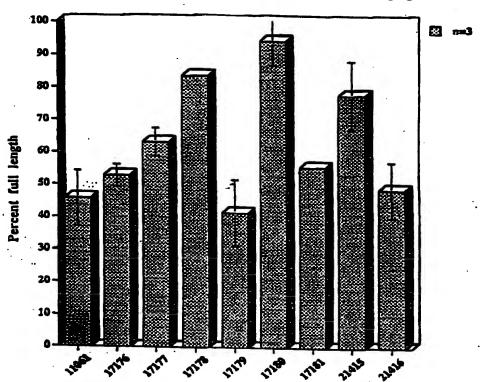


Figure \$ 4

Docket No. 4789 Appln. No: Not yet assigned
Title: Oligoeotides Having A-DNA Form and B-DNA

Conformational Geometry Inventor(s): Manoharan, et al

Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 5 of 9

FFECT OF CHEMICAL MODIFICATION ON THE STABILITY OF ISIS 11061 ONGENORS IN MOUSE TISSUE (100 mg) 24 HRS AFTER 5 mg/kg IV BOLUS.

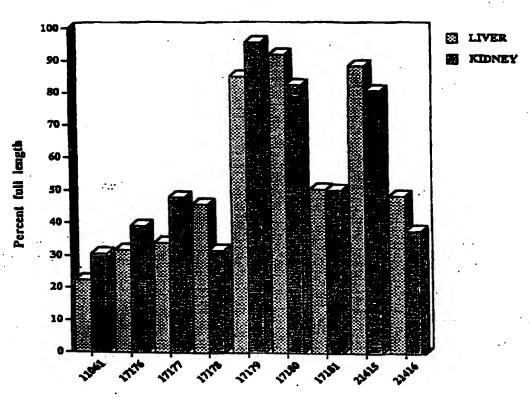


Figure \$ 5

Docks ISIS-4789 Appln. No: Not yet assigned
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Conformational Geometry Inventor(s): Manoharan, et al

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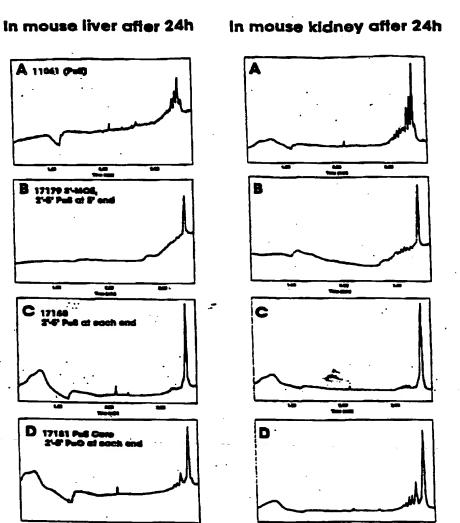


Figure 6 6

C-RAF MRNA EXPRESSION IN DENU CELLS DOSE RESPONSE WITH MOE (2'-5' LINKED) 11061 ANALOGS 21415 17181 17180 17179 200nm 17178 17177 17176 100nm 11061 8 8 各 120 8 8 C-RAF mRNA (%control)

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Title: Oligonucleotides Having A-DNA Form and B-DNA Form

Appln. No: Not yet assigned

Attorney: Emma R. Dailey Inventor(s): Manoharan, et al Conformational Geometry

Docket No.: 1S1S-4789

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OLIGO

Scrambled control, P=S Positive control, P=S MMI (1+1), P=S MMI (2+2), P=S MMI (3+3), P=S MMI (2+2), P=0 MMI (3+3), CATCGCTCCTCAGGG CATCGCTCCITCAGGG CEGICATCGCTCCTCAGEG CENCATCGCTCCTCRGGG **CCGTCATCGCTCCTCAGGG** TAGTAATAGCCCCACATGG 1-00651 ISIS 14899 ISIS 14897 ISIS 14890 ISIS 14896 ISIS 14898 13177 **ISIS 1**

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Title: Oligonucleorides Having A-DNA Form and B-DNA Form

Appln. No: Not yet assigned

Attorney: Emma R. Dailey Inventor(s): Manoharan, et al Conformational Geometry

Docket No.: 1515-4789

Docket No.: ISIS-4789 Appln. No: Not yet assigned
Title: Oligonucleotides Having A-DNA Form and B-DNA Form
Conformational Geometry
Inventor(s): Manoharan, et al
Attorney: Emma R. Dailey Phone No.: 215-568-3100 Sheet 9 of 9

